SEQUENCE LISTING

<110> Ferrell, Robert E. Alitalo, Kari Finegold, David N Karkkainen, Marika <120> SCREENING AND THERAPY FOR LYMPHATIC DISORDERS INVOLVING THE FLT4 RECEPTOR TYROSINE KINASE (VEGFR-3) <130> 28967/35255A <140> <141> <150> PCT/US99/06133 -<151> 1999-03-26 <160> 28 <170> PatentIn Ver. 2.0 <210> 1 <211> 4111 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (20) . . (4111) <223> Human Flt4 (VEGFR-3) long form cDNA <400> 1 ccacgcgcag cggccggag atg cag cgg ggc gcc gcg ctg tgc ctg cga ctg Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu 10 tog etc tge etg gga etc etg gae gge etg gtg agt gge tae tee atg Trp Leu Cys Leu Gly Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met 15 acc ccc ccg acc ttg aac atc acg gag gag tca cac gtc atc gac acc 148 Thr Pro Pro Thr Leu Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr 35 30 ggt gac agc ctg tec atc tec tgc agg gga cag cac eec etc gag tgg 196 Gly Asp Ser Leu Ser Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp 50 get tgg eca gga get cag gag geg eca gee ace gga gae aag gae age Ala Trp Pro Gly Ala Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser 75 70 60 65

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Gly Gly C	tgc tgc aat Cys Cys Asn 165	agt gag ggg Ser Glu Gly 170	ctg cag tgc Leu Gln Cys	atg aac acc Met Asn Thr 175	agc acg 885 Ser Thr
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ggc Gly 195	ccc Pro	aaa Lys	cca Pro	gta Val	aca Thr 200	atc Ile	agt Ser	ttt Phe	gcc Ala	aat Asn 205	cac His	act Thr	tcc Ser	tgc Cys	cga Arg 210	981
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150

165

Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn Thr

170

Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro Leu 185 180 Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr Ser 200 Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser Ile 215 Ile Arg Arg Ser Leu Pro Ala Thr Leu Pro Gln Cys Gln Ala Ala Asn 230 Lys Thr Cys Pro Thr Asn Tyr Met Trp Asn Asn His Ile Cys Arg Cys 250 . 245 Leu Ala Gln Glu Asp Phe Met Phe Ser Ser Asp Ala Gly Asp Asp Ser 270 265 Thr Asp Gly Phe His Asp Ile Cys Gly Pro Asn Lys Glu Leu Asp Glu 280 285 275 Glu Thr Cys Gln Cys Val Cys Arg Ala Gly Leu Arg Pro Ala Ser Cys 295 300 Gly Pro His Lys Glu Leu Asp Arg Asn Ser Cys Gln Cys Val Cys Lys 315 320 310 305 Asn Lys Leu Phe Pro Ser Gln Cys Gly Ala Asn Arg Glu Phe Asp Glu 330 325 Asn Thr Cys Gln Cys Val Cys Lys Arg Thr Cys Pro Arg Asn Gln Pro 345 Leu Asn Pro Gly Lys Cys Ala Cys Glu Cys Thr Glu Ser Pro Gln Lys 360 355 Cys Leu Leu Lys Gly Lys Lys Phe His His Gln Thr Cys Ser Cys Tyr 375 380 Arg Arg Pro Cys Thr Asn Arg Gln Lys Ala Cys Glu Pro Gly Phe Ser 395 385 390 Tyr Ser Glu Glu Val Cys Arg Cys Val Pro Ser Tyr Trp Lys Arg Pro

410

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gctg	rcctg	rat <u>c</u>	jtcaa	actgo	et ta	igtaa	tcac	j tgg	gatat	tga	aata	ittca		atg t Met T	ac Yr	416
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														agt Ser	ttg Leu 50	560
														tgg Trp 65	aga Arg	- 608
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														cct Pro		752
	Thr													aac Asn		800
														tgt Cys 145		848

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	Pro			cca Pro												1040
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Lèu [.]	Āla	Gly 245	Thr	gaa Glu	Asp	His	Ser 250	His	Leu	Gln	Glu	Pro 255	Ala	Leu	Cys	1184
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				aaa Lys												1280
				gaa Glu 295												1328
				acc Thr												1376
aga Arg	cca Pro	tgt Cys 325	gca Ala	agt Ser	ggc	aaa Lys	aca Thr 330	gca Ala	tgt Cys	gca Ala	aag Lys	cat His 335	tgc Cys	cgc Arg	ttt Phe	1424
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Ser Leu Glu Glu Leu Leu Arg Ile Thr His Ser Glu Asp Trp Lys Leu 50 55 60

Trp Arg Cys Arg Leu Arg Leu Lys Ser Phe Thr Ser Met Asp Ser Arg 65 70 75 80

Ser Ala Ser His Arg Ser Thr Arg Phe Ala Ala Thr Phe Tyr Asp Ile 85 90 95

Glu Thr Leu Lys Val Ile Asp Glu Glu Trp Gln Arg Thr Gln Cys Ser 100 105 110

Pro Arg Glu Thr Cys Val Glu Val Ala Ser Glu Leu Gly Lys Ser Thr 115 120 125

Asn Thr Phe Phe Lys Pro Pro Cys Val Asn Val Phe Arg Cys Gly Gly
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Cys Cys Asn Glu Glu Ser Leu Ile Cys Met Asn Thr Ser Thr Ser Tyr
145 150 155 160

Ile Ser Lys Gln Leu Phe Glu Ile Ser Val Pro Leu Thr Ser Val Pro 165 Glu Leu Val Pro Val Lys Val Ala Asn His Thr Gly Cys Lys Cys Leu 185 Pro Thr Ala Pro Arg His Pro Tyr Ser Ile Ile Arg Arg Ser Ile Gln 200 Ile Pro Glu Glu Asp Arg Cys Ser His Ser Lys Lys Leu Cys Pro Ile Asp Met Leu Trp Asp Ser Asn Lys Cys Lys Cys Val Leu Gln Glu Glu 230 Asn Pro Leu Ala Gly Thr Glu Asp His Ser His Leu Gln Glu Pro Ala 250 245 Leu Cys Gly Pro His Met Met Phe Asp Glu Asp Arg Cys Glu Cys Val 265 260 Cys Lys Thr Pro Cys Pro Lys Asp Leu Ile Gln His Pro Lys Asn Cys 280 Ser Cys Phe Glu Cys Lys Glu Ser Leu Glu Thr Cys Cys Gln Lys His . 300 290 Lys Leu Phe His Pro Asp Thr Cys Ser Cys Glu Asp Arg Cys Pro Phe 310 315 His Thr Arg Pro Cys Ala Ser Gly Lys Thr Ala Cys Ala Lys His Cys 330 . 325 Arg Phe Pro Lys Glu Lys Arg Ala Ala Gln Gly Pro His Ser Arg Lys 345 340

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Asn Ile Thr Glu Asp Ser Tyr Val Ile Asp Thr Gly Asp Ser Leu Ser	
35 40 45	
Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Thr Trp Pro Gly Ala	•
50 55 60	
Gln Glu Val Leu Thr Thr Gly Gly Lys Asp Ser Glu Asp Thr Arg Val	
65 70 75 80	•
Val His Asp Cys Glu Gly Thr Glu Ala Arg Pro Tyr Cys Lys Val Leu	
85 90 95	
Leu Leu Ala Gln Thr His Ala Asn Asn Thr Gly Ser Tyr His Cys Tyr	
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Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Thr	•
115 120 125	
Tyr Val Phe Val Arg Asp Phe Lys His Pro Phe Ile Asn Lys Pro Asp	
130 135 140	
Thr Leu Leu Val Asn Arg Lys Asp Ser Met Trp Val Pro Cys Leu Val	
145 150 155 160	

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440

435

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- Asp Gly Met Pro Gln Cys Arg Asp Trp Lys Glu Val Thr Thr Gln Asp 485 490 495
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- Gly Lys Asn Lys Thr Val Ser Lys Leu Val Ile Gln Asp Ala Asn Val 515 520 525
- Ser Ala Met Tyr Lys Cys Val Val Val Asn Lys Val Gly Gln Asp Glu 530 535 540
- Arg Leu Ile Tyr Phe Tyr Val Thr Thr Ile Pro Asp Gly Phe Ser Ile 545 550 555 560
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- Asp Cys Lys Asn Val His Leu Phe Ala Thr Pro Leu Glu Ala Asn Leu 610 615 620
- Glu Glu Ala Glu Pro-Gly Ala Arg His Ala Thr Leu Ser Leu Asn Ile 625 630 635 ~640
- Pro Arg Val Ala Pro Glu Asp Glu Gly Asp Tyr Val Cys Glu Val Gln
 645 650 655
- Asp Arg Arg Ser Gln Asp Lys His Cys His Lys Lys Tyr Leu Ser Val 660 665 670
- Gln Ala Leu Glu Ala Pro Arg Leu Thr Gln Asn Leu Thr Asp Leu Leu 675 680 685
- Val Asn Val Ser Asp Ser Leu Glu Met Arg Cys Pro Val Ala Gly Ala 690 695 700
- His Val Pro Ser Ile Val Trp Tyr Lys Asp Glu Arg Leu Leu Glu Lys 705 710 715 720
- Glu Ser Gly Ile Asp Leu Ala Asp Ser Asn Gln Arg Leu Ser Ile Gln
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Glu	Asp 770	Lys	Gly	Ser	Met	Glu 775	Ile	Val	Ile	Leu	Ile 780	Gly	Thr	Gly	Val
Ile 785	Ala	Val	Phe	Phe	Trp 790	Val	Leu	Leu	Leu	Leu 795	Ile	Phe	Cys	Asn	Met 800
Lys	Arg	Pro	Ala	His 805	Ala	Asp	Ile	Lys	Thr 810	Gly	Tyr	Leu	Ser	11e 815	Ile
Met	Asp:	Pro	Gly 820	Glu	Val	Pro	Leu	Glu 825	Glu	Gln	Cys	Glu	Tyr 830	Leu	Ser
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			Leu 900				. `_	905					910		
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-	930		Tyr			935			-		940				. :
945		,	Pro		950					955					960
	٠		Val	965					970					975	•
			Ala 980					985					990		
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- Arg Asn Ile Leu Leu Ser Glu Ser Asp Ile Val Lys Ile Cys Asp Phe 1045 1050 1055
- Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val Arg Lys Gly
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- Lys Val Tyr Thr Thr Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu 1090 1095 1100
- Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Gln Ile 1105 1110 1115 1120
- Asn Glu Glu Phe Cys Gln Arg Leu Lys Asp Gly Thr Arg Met Arg Ala 1125 1130 1135
- Pro Glu Leu Ala Thr Pro Ala Ile Arg His Ile Met Gln Ser Cys Trp 1140 1145 1150
- Ser Gly Asp Pro Lys Ala Arg Pro Ala Phe Ser Asp Leu Val Glu Ile 1155 1160 1165
- Leu Gly Asp Leu Leu Gln Gly Gly Gly Trp Gln Glu Glu Glu Glu 1170 1175 1180
- Arg Met Ala Leu His Ser Ser Gln Ser Ser Glu Glu Asp Gly Phe Met 1185 1190 1195 1200
- Gln Ala Ser Thr Thr Ala Leu His Ile Thr Glu Ala Asp Ala Asp Asp 1205 1210 1215
- Ser Pro Pro Ser Met His Cys His Ser Leu Ala Ala Arg Tyr Tyr Asn 1220 1225 1230
- Cys Val Ser Phe Pro Gly Arg Leu Ala Arg Gly Thr Lys Thr Pro Gly 1235 1240 1245
- Ser Ser Arg Met Lys Thr Phe Glu Glu Leu Pro Met Thr Pro Thr Thr 1250 1255 1260
- Tyr Lys Ala Ser Met Asp Asn Gln Thr Asp Ser Gly Met Val Leu Ala 1265 1270 1275 1280
- Ser Glu Glu Phe Glu Glu Leu Glu Ser Arg His Arg Pro Glu Gly Ser 1285 1290 1295
- Phe Ser Cys Lys Gly Pro Gly Gln His Met Asp Ile Pro Arg Gly His 1300 1305 1310

Pro Asp Pro Gln Gly Arg Arg Arg Pro Thr Gln Gly Ala Gln Gly 1315 Gly Lys Val Phe Tyr Asn Asn Glu Tyr Gly Glu Val Ser Gln Pro Cys 1335 Thr Glu Gly Asp Cys Cys Pro Ser Ala Gly Ser Thr Phe Phe Ala Asp 1350 Ser Ser Tyr <210> 20 <211> 21 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: oligonucleotide <400> 20 cggcgccttc aggaaggtgg t <210> 21 <211> 21 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: oligonucleotide <400> 21 cggaacattc cgctgtcgga a <210> 22 <211> 21 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: oligonucleotide <400> 22 gtcggaaagc aacgtggtga a 21 <210> 23 <211> 18

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